

DEMARKO	•				SE	QUENC	CE L	ISTI	NG					
<110>	Bond	, Chi	risto	per	J.									
<120>	SYNT	HETI	C AN'	гівоі	OY PI	HAGE	LIBI	RARII	ES					
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<220> <223>	4D5	light	t cha	ain v	/aria	able	doma	ain						
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Asp Arg	g Val	Thr 20	Ile	Thr	Cys	Arg	Ala 25	Ser	Gln	Asp	Val	Asn 30	Thr	Ala
Val Ala	a Trp 35	Tyr	Gln	Gln	Lys	Pro 40	Gly	Lys	Ala	Pro	Lys 45	Leu	Leu	Ile
Tyr Se:	r Ala	Ser	Phe	Leu	Glu 55	Ser	Gly	Val	Pro	Ser 60	Arg	Phe	Ser	Gly
Ser Arg	g Ser	Gly	Thr	Asp 70	Phe	Thr	Leu	Thr	Ile 75	Ser	Ser	Leu	Gln	Pro 80
Glu Ası	p Phe	Ala	Thr 85	Tyr	Tyr	Cys	Gln	Gln 90	His	Tyr	Thr	Thr	Pro 95	Pro

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr 100 $$ 105

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<213> Artificial Sequence

<220>

<223> 4D5 heavy chain variable domain

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Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile Lys Asp Thr 20 25 30

Tyr Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Arg Ile Tyr Pro Thr Asn Gly Tyr Thr Arg Tyr Ala Asp Ser Val 50 60

Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr 65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ser Arg Trp Gly Gly Asp Gly Phe Tyr Ala Met Asp Val Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser 115 120

<210> 3

<211> 35

<212> PRT

<213> Artificial Sequence

<220>

<223> GNC4 leucine zipper

<400> 3

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Asn Tyr His Leu Glu Asn Glu Val Ala Arg Leu Lys Lys Leu Val Gly
20 25 30

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Glu Arg Gly
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Tyr Ala Met Asp Tyr
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Ser Arg Asn Ala Trp Ala Phe
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<223> F63
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<223> F65
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<223> Xaa is any naturally occurring amino acid
<400> 11
Ser Arg Xaa Xaa Xaa Xaa Xaa Xaa Tyr Ala Met Asp Tyr
<210> 12
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<212> PRT
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<223> F64
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      (3)..(7)
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<222> (25)..(26)
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<222> (28)..(28)
<223> w is a or t
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<222> (29)..(29)
<223> m is a or c
<220>
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<222> (30)..(30)
<223> y is c or t
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<222> (31)..(31)
<223> k is g or t
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                                                                     51
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<222> (22)..(22)
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<223> d is a, g, or t
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<223> r is a or g
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<221> misc_feature
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<223> d is a, g, or t
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<222> (44)..(44)
<223> m is a or c
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<222> (49)..(49)
<223> d is a, g, or t
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                                                                     72
agcgtcaagg gc
<210> 17
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<222> (22)..(22)
<223> d is a, g, or t
<220>
<221> misc_feature
<222> (23)..(23)
<223> h is a, c, or t
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<220>
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<222> (28)..(28)
<223> w is a or t
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<221> misc feature
\langle 222 \rangle (29)..(29)
<223> m is a or c
<220>
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<222> (34)..(34)
<223> d is a, g, or t
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<222> (35)..(35)
<223> m is a or c
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<223> r is a or g
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<221> misc_feature
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<223> m is a or c
<220>
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<222> (49)..(49)
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                                                                       72
agcgtcaagg gc
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<211> 1441
<212> DNA
<213> Artificial Sequence
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<223> single chain Fv
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                                                                      120
aggaccatag attatgaaaa taaaaacagg tgcacgcatc ctcgcattat ccgcattaac
                                                                      180
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gacgatgatg	ttttccgcct	cggcttatgc	atccgatatc	cagatgaccc	agtccccgag	240
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gaatactgct	gtagcctggt	atcaacagaa	accaggaaaa	gctccgaagc	ttctgattta	360
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tcaagtcggt	gacggtgata	attcaccttt	aatgaataat	ttccgtcaat	atttaccttc	1260
cctccctcaa	tcggttgaat	gtcgcccttt	tgtctttagc	gctggtaaac	catatgaatt	1320
ttctattgat	tgtgacaaaa	taaacttatt	ccgtggtgtc	tttgcgtttc	ttttatatgt	1380
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a						1441

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<213> Artificial Sequence

<220>

<223> single chain Fv with zipper domain

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aggaccatag attatgaaaa taaaaacagg tgcacgcatc ctcgcattat ccgcattaac 180

gacgatgatg	ttttccgcct	cggcttatgc	atccgatatc	cagatgaccc	agtccccgag	240
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gaatactgct	gtagcctggt	atcaacagaa	accaggaaaa	gctccgaagc	ttctgattta	360
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ggatttcact	ctgaccatca	gcagtctgca	gccggaagac	ttcgcaactt	attactgtca	480
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11

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<212> DNA

<213> Artificial Sequence

<220>

<223> Fab fragment

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ctccctgtcc	gcctctgtgg	gcgatagggt	caccatcacc	tgccgtgcca	gtcaggatgt	300
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<210> 21

<211> 2383

<212> DNA

<213> Artificial Sequence

<220>

<223> Fab fragment with zipper domain

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                                                                     1260
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                                                                     1320
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Thr Asn Asp Tyr Tyr
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Thr Thr Ser Tyr Gly
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Ala Ser Ser Tyr Ser Tyr Arg
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Ala Lys Trp Arg Thr Ser Trp Lys Tyr
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Thr Asn Gly Asn Tyr
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Gly Trp Ser Asn Gly Tyr Arg
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Ala Trp Ser Tyr Asn Tyr Arg
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Thr Gly Asn Ser Trp
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<212> PRT
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<400> 108

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Asn Gly Lys Ser Ser
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Trp Ser Tyr Glu Ala Ala
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Thr Ser Trp Ser Lys Pro Tyr
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Val Thr Tyr Asp Asp Thr
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Thr Gly Gly Ser Trp
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Val Tyr Thr Tyr Tyr Asp

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Trp Gly Ser Gly Tyr Thr Trp
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<210> 130

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Leu Ala Tyr Ala Tyr Asn
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Val Tyr His Asp Lys Tyr
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                                                                      60
cctgtgctgc ctcgggtcgt actggttcta cttatqatat qqqctqqttt cqtcaqqctc
                                                                     120
cgggtaaaga acgtgaatcg gttgccgcca ttaactggga ttcggctcgt acttactatg
                                                                     180
cttcgtccgt ccgtggtcgt tttactattt cacgtgataa tgccaaaaaa actgtctatt
                                                                     240
tgcagatgaa ttcattgaaa ccagaagata ctgccgtcta tacttgtggt gctggtgaag
                                                                     300
geggtaettg ggattettgg ggteagggta ceeaggteae tgteteetet geeggtggta
                                                                     360
tggattataa agatgatgat gataaatga
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<210> 136
<211> 129
<212> PRT
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Asp Val Gln Leu Gln Glu Ser Gly Gly Leu Val Gln Ala Gly Gly
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Arg Thr Gly Ser Thr Tyr
Asp Met Gly Trp Phe Arg Gln Ala Pro Gly Lys Glu Arg Glu Ser Val
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Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Lys Thr Val Tyr

Ala Ala Ile Asn Trp Asp Ser Ala Arg Thr Tyr Tyr Ala Ser Ser Val

55

50

Leu Gln Met Asn Ser Leu Lys Pro Glu Asp Thr Ala Val Tyr Thr Cys
85 90 95

Gly Ala Gly Glu Gly Gly Thr Trp Asp Ser Trp Gly Gln Gly Thr Gln
100 105 110

Val Thr Val Ser Ser Ala Gly Gly Met Asp Tyr Lys Asp Asp Asp Asp 115 120 125

Lys

<210> 137

<211> 23

<212> PRT

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<223> CDRH3 17 amino acid insert

<220>

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<223> Xaa is any naturally occurring amino acid

- - - .

<400> 137

Xaa Xaa Xaa Xaa Trp Gly

<210> 138

<211> 4

<212> PRT

<213> Artificial Sequence

<220>

<223> VHH RIG N terminal sequence

<220>

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<223> Xaa is any naturally occurring amino acid

<400> 138

Arg Ile Xaa Cys

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1
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Cys Trp Val Thr Trp
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<220>
<221> MISC FEATURE
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<223> Xaa is W, G, R, M, S, or A
<220>
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<223> Xaa is V, L, P, G, S, E or W
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5
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                                                   15
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Xaa Xaa Xaa Xaa Xaa 20

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<223> Xaa is I, L, V, R, W or S
<220>
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<223> Xaa is any naturally occurring amino acid, wherein there can be 1
      or more deletions up to 16 deletions
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<223> Xaa is W, G, R, M, S, or A
<220>
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<222> (21)..(21)
<223> Xaa is V, L, P, G, S, E or W
<220>
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<222> (22)..(23)
<223> Xaa is any naturally occurring amino acid;
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5
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Xaa Xaa Xaa Xaa Xaa Xaa
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<223> Xaa is R, L, or V
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<223> Xaa is I, L, or V
<220>
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<222> (3)..(19)
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<223> Xaa is any naturally occurring amino acid;
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<223> Xaa is W, G, R, or M
<220>
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<223> Xaa is V, L, or P
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5
Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
          20
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<221> MISC_FEATURE
<222> (5)..(24)
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10
Xaa Xaa Xaa Xaa Xaa Xaa Xaa
          20
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<220>
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<222> (21)..(21)
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<220>
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<223> Xaa is any naturally occurring amino acid
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Xaa Trp Xaa Xaa Xaa Xaa
         20
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5
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Xaa
<210> 146
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<223> Xaa is any naturally occurring amino acid
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<223> Xaa is any naturally occurring amino acid
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<221> MISC FEATURE
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               5
                                   10
Xaa
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Arg Leu Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Trp Xaa Xaa Xaa Xaa
Xaa
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                                                                     60
nnsnnsnnsn nsnnstgggg tcagggt
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kccksggytr ctksgtgggg tcagggt
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rctsstgyts makcctgggg tcagggt
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      (74)...(74)
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                                                                      87
kytgstsytg ytgsttgggg tcagggt
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gmarygscas ytgcgtgggg tcaggg
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Trp
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Ser
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                                   10
Ala
<210> 168
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Val Leu Glu Leu Arg Ser Ser Gly Gly Asn Ala Arg Trp Met Ser Leu
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Tyr
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                                   10
Tyr
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Leu Trp Thr Arg Ala Arg Ser Trp Arg Trp Trp Trp Arg Arg Glu Gln
                                   10
Phe
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10

Ala

<210> 172

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Ser
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Ala Xaa Xaa Xaa Trp Xaa Xaa Xaa Tyr Ala Met Asp Tyr
                5
                                    10
<210> 174
<211> 13
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               5
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                                  10
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Tyr
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                                 10
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           20
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Arg Ile Xaa Cys Xaa Xaa Xaa Xaa Xaa Cys Trp Val Xaa Xaa

1 5 10 15